EDISON

Oryzon Genomics

Q316 results update

Fresh preclinical ORY-2001 data, ORY-1001 next

Pharma & biotech

Oryzon's Q316 update revealed good progress on R&D and it reiterated that the preliminary Phase I/IIa data for ORY-1001 is expected to be presented at the American Society of Hematology (ASH) annual meeting on 3 to 6 December 2016. The focus will be on Part 2 of the study, which should include preliminary efficacy information. Oryzon has also made progress with earlier R&D projects, with fresh preclinical ORY-2001 data in September demonstrating potential in a new multiple sclerosis indication, and revealed, in July, a third product, ORY-3001, targeting undisclosed non-oncological indications. Our Oryzon valuation is virtually unchanged at €156m or €5.5/share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/14	15.5	11.3	0.48	0.0	N/A	N/A
12/15	7.2	(0.1)	(0.01)	0.0	N/A	N/A
12/16e	4.8	(4.9)	(0.16)	0.0	N/A	N/A
12/17e	2.8	(6.2)	(0.22)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

Q316 results and additional debt financing

Oryzon reported its Q316 results on 24 October. Converted into its functional currency, R&D expenses were €1.3m, up from €0.9m a year ago due to increased overall activity. G&A costs of €1.2m in Q316 were higher year-on-year, in line with our expectations and reflected increased headcount and compliance costs. Solid cash and term deposits of €28.6m (net cash of €3.6m) at the end of Q316 were significantly boosted with additional debt of €5.3m from a second tranche in September following the first tranche of €10.5m in May 2016. The loans are long-term, non-senior, non-convertible carrying current commercial interest rates.

Focus Phase I/IIa readout and next steps

Oryzon reiterated that it expects to announce the preliminary data from the Phase I/IIa trial with ORY-1001 at ASH in December, which is a key milestone in the near term. The study includes different subsets of acute leukaemia patients treated with ORY-1001, lysine specific demethylase 1 (LSD1) inhibitor. The trial consisted of two arms, with Part 1 demonstrating preliminary safety and tolerability. Part 2 will provide preliminary efficacy data in December. ORY-1001 has been partnered with Roche since April 2014. After completion of the ongoing Phase I/IIa, Roche will be solely responsible for further clinical development and commercialisation of ORY-1001, which could expand beyond acute leukaemia.

Valuation: €156m or €5.5/share

We value Oryzon at a virtually unchanged €156m (previously €158m) or €5.5/share. Our valuation has been updated for slightly lower net cash, offset by rolling our model forward. The upcoming Phase I/IIa data could provide a catalyst for value inflection.

3 November 2016

Price	**€2.90**
Market cap	**€83m**

Net cash (€m) at end of Q316	3.6
Shares in issue	28.5m
Free float	30%
Code	ORY
Primary exchange	Madrid Stock Exchange
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	3.6	0.0	N/A
Rel (local)	2.1	(6.7)	N/A
52-week high/low		€4.60	€2.60

Business description

Oryzon Genomics is a Spanish biotechnology company focused on developing novel epigenetic compounds. Lead compound ORY-1001 is partnered with Roche and is undergoing a Phase I/IIa study for acute leukaemia. ORY-2001 has potential for Alzheimer's disease and has entered Phase I. ORY-3001 is a new preclinical asset.

Next events

ORY-1001 Phase I/IIa results	Dec 2016 (ASH)
ORY-2001 Phase I results	H117

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Edison profile page

Preclinical POC of ORY-2001 in multiple sclerosis

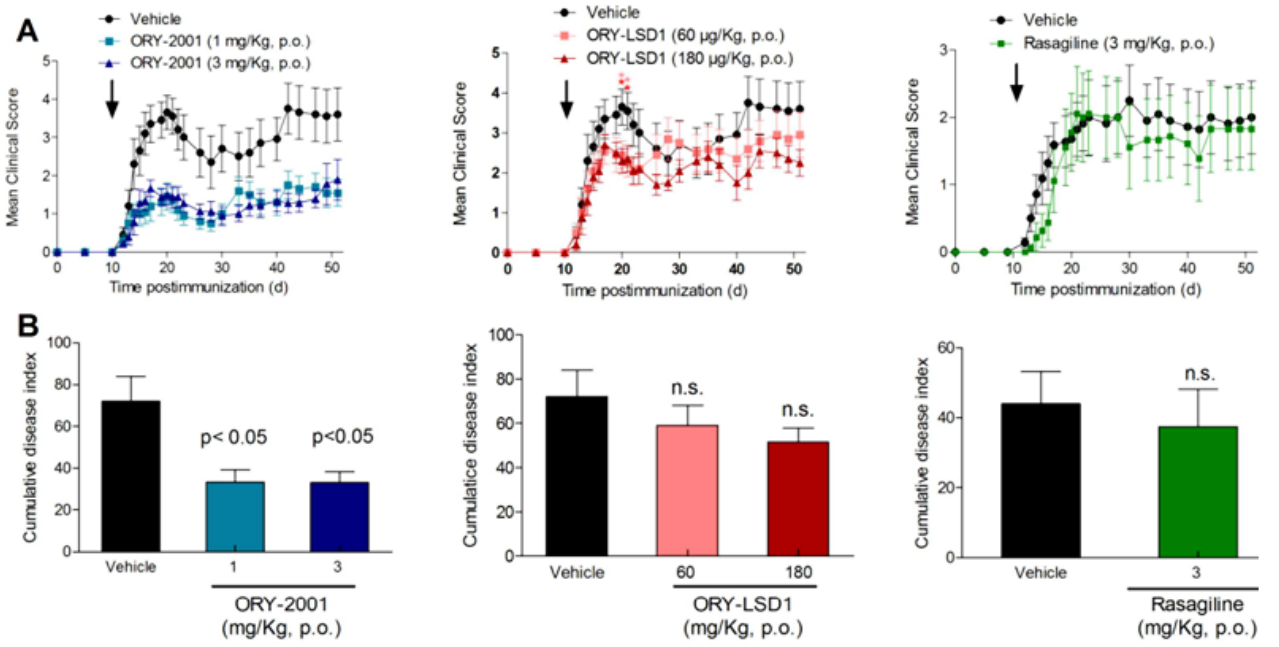
ORY-2001 (dual LSD1 and monoamine oxidase B inhibitor), which is being developed for Alzheimer's disease (AD), entered a Phase I trial in Q116 with healthy volunteers to establish safety/tolerability. As guided previously, Phase II with AD patients could start in H117.

In September 2016 Oryzon presented fresh preclinical ORY-2001 data in poster format (full data unpublished) at the 32nd congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS). ORY-2001 was tested in a preclinical proof-of-concept (POC) trial using a multiple sclerosis (MS) mouse model. MS emerged as a second potential indication for ORY-2001, which is still wholly owned by the company.

So far, ORY-2001 has demonstrated efficacy in preclinical dementia models but, following the insights from biomarker analysis showing ORY-2001's downregulating effect on neuroinflammatory genes, including S100A9, Oryzon conducted the present study with ORY-2001 in an experimental autoimmune encephalomyelitis (EAE) mice model, a widely used proxy for MS, which has been shown to have upregulated S100A9.

The study included three controlled arms: EAE mice treated with ORY-2001 (dual LSD1/MAO-B inhibitor), ORY-LSD1 (proprietary selective LSD1 inhibitor) or rasagiline (widely used selective MAO-B inhibitor; MAO-B is a well-established target in certain CNS conditions). The data showed that treatment with ORY-2001 effectively reduced the severity of the disease (Exhibit 1, A) and cumulative disease index (Exhibit 1, B). Dual inhibition of LSD1/MAO-B with ORY-2001 was more effective than standalone inhibition of LSD1 with ORY-LSD1 or MAO-B with rasagiline. Oryzon is yet to provide further development plans for this indication, but should the company move ORY-2001 into the clinic this will be a new, first-in-class approach for MS.

Exhibit 1: Effects of the treatment with ORY-2001, ORY-LSD1 and rasagiline in EAE mice model



Source: T. Maes et al. LSD1 inhibition, a potential epigenetic therapeutic approach for the treatment of Multiple Sclerosis. Poster presentation, 32nd congress of the European Committee for Treatment and Research in Multiple Sclerosis, September 2016. Note: Cumulative disease index = the sum of clinical scores reached for each animal every day until day 51 post-immunization.

MS market potential

Around 400k people are diagnosed with MS in the US each year and around 85% of those have a relapsing-remitting course of the disease, which is in contrast to the progressive type, when symptoms gradually get worse over time rather than appearing as relapses. The mainstay of the treatment is disease-modifying therapies with the goal of reducing the frequency of relapses and slowing progression (source: Multiple Sclerosis, Medscape) with Evaluate Pharma estimating that the market will be worth $25bn in 2020. MS remains a highly debilitating disease, eventually incapacitating the patients, and is still an unmet medical need.

Valuation

Our valuation of Oryzon is virtually unchanged at €156m or €5.5/share, based on a risk-adjusted NPV analysis, which includes €1.2m net cash at end 2016. We do not include the MS indication for ORY-2001 in our valuation yet, although we clearly see the differentiation of this asset in terms of mechanism of action. We will revisit ORY-2001 for MS when more details have emerged or upon Oryzon's decision to proceed with this indication into the clinic. Fine-tuning our near-term forecasts did not significantly affect our long-term product forecasts or valuation. Rolling out model forward by one quarter mostly offset the decrease in the net cash position (with the new debt). We use a 12.5% discount rate, with probabilities for reaching the market of 15% and 12% for ORY-1001 and ORY-2001, respectively.

Exhibit 2: Oryzon rNPV valuation

Product	Indication	Launch	Peak sales (US$m)	Value (€m)	Probability (%)	rNPV (€m)	NPV/share (€/share)
ORY-1001	AML	2022	900	246.8	15%	44.0	1.5
ORY-1001	SCLC	2025	630*	116.9	8%	16.5	0.6
ORY-2001	AD	2026	4,510*	778.1	12%	94.3	3.3
Net cash (end-2016)				1.2	100%	1.2	0.0
Valuation				1,143.0		156.1	5.5

Source: Edison Investment Research. Note: *Peak sales are rounded to the nearest US$10m, shown in US$. SCLC = small cell lung cancer; AML = acute myeloid leukaemia; AD = Alzheimer's disease.

Currently, our valuation is based on clinical-stage compounds and one preclinical indication (Exhibit 2). ORY-1001 has been partnered with Roche since April 2014 (for deal details see our previous report). After completion of the ongoing Phase I/IIa, Roche will be solely responsible for further clinical development and commercialisation of ORY-1001, and could expand it beyond acute leukaemia. Specifically, we include ORY-1001 to be developed for small cell lung cancer (SCLC) because, in our view, this indication appears to be the most likely one for Roche to expand. ORY-2001 is still unpartnered, but Oryzon's strategy is to develop the asset until clinical POC stage and then seek to out-license it. We have assumed a licensing deal for this asset in our model (see our initiation report for more details).

Financials

In Q316 Oryzon's revenues of €0.2m consisted of a reimbursement payment from Roche according to the R&D collaboration agreement, which is separate to the ORY-1001 licensing deal. Earlier in 2016, the company fully recognized deferred income after a milestone payment of $4m from Roche in July 2015, which therefore resulted in lower collaboration revenues y-o-y (€0.7m in Q315). The R&D collaboration agreement with Roche was extended in April 2016 to March 2017. In addition, in Q316 the company recorded income of €1.2m to account for the capitalisation of the development costs (€2.9m in 2016 so far). Oryzon follows Spanish GAAP and research costs are expensed, while development costs can be capitalised by recognising income in the P&L statement.

We have revised our near-term financial forecasts, while our projections for Oryzon's products remain unchanged; therefore our revised estimates did not have a significant effect on our valuation. The increase in 2016 and 2017 revenue estimates comes from a slightly higher Roche reimbursement level than we previously expected and higher Oryzon's R&D cost projections, which allow for more spending to be capitalised, as explained above. The increase in our R&D cost estimates mostly reflects higher overall activity, especially with ORY-2001, but also the preclinical development with a new candidate, ORY-3001, undergoing for toxicological studies. G&A costs of €1.2m in Q316 were higher year-on-year, in line with our expectations and reflected increased headcount and compliance costs. The net effect on our loss per share estimates was slightly negative, from €0.18 to €0.19 in FY16 and from €0.23 to €0.25 in FY17.

Following the addition of the new debt, we forecast a comfortable 2016 year-end cash position of €29.5m (cash and term deposits classed as other current assets). In total, during the past 12-18 months Oryzon has managed to attract more than €32m in new funding from various sources. In addition, it has a history of efficient use of available public grants, which could provide further non-dilutive financing.

Exhibit 3: Key changes to our financial forecasts

€m	2015	2016e			2017e		
	Actual	Old	New	Change (%)	Old	New	Change (%)
Revenue	7.185	3.886	4.835	+24%	2.467	2.797	+13%
Gross profit	7.185	3.886	4.835	+24%	2.467	2.797	+13%
Operating profit (reported)	(0.233)	(4.612)	(4.715)	+2%	(5.590)	(6.281)	+12%
Profit before tax (reported)	(0.955)	(5.474)	(5.708)	+4%	(6.433)	(7.124)	+11%
Profit after tax (reported)	(0.992)	(5.107)	(5.312)	+4%	(6.433)	(7.124)	+11%
EPS reported (€)	(0.04)	(0.18)	(0.19)	+4%	(0.23)	(0.25)	+11%

Source: Oryzon accounts, Edison Investment Research

Exhibit 4: Financial summary

€'000s	2012	2013	2014	2015	2016e	2017e
December	Local GAAP	Local GAAP	Local GAAP	Local GAAP	Local GAAP	Local GAAP
PROFIT & LOSS						
Revenue	4,353	2,360	15,536	7,185	4,835	2,797
Cost of Sales	0	0	0	0	0	0
Gross Profit	4,353	2,360	15,536	7,185	4,835	2,797
Research and development	(876)	(873)	(1,108)	(3,191)	(4,783)	(3,774)
EBITDA	856	(94)	11,659	688	(3,780)	(5,260)
Operating Profit (before amort. and except.)	559	(370)	11,398	448	(3,898)	(5,378)
Intangible Amortisation	(455)	(657)	(657)	(657)	(817)	(902)
Exceptionals	0	(186)	(4,617)	(24)	0	0
Other	0	0	0	0	0	0
Operating Profit	104	(1,213)	6,124	(233)	(4,715)	(6,281)
Exceptionals	(220)	0	667	(169)	0	0
Net Interest	(582)	(672)	(52)	(553)	(993)	(843)
Profit Before Tax (norm)	(23)	(1,042)	11,346	(105)	(4,891)	(6,221)
Profit Before Tax (reported)	(698)	(1,885)	6,739	(955)	(5,708)	(7,124)
Tax	90	89	(88)	(37)	396	0
Profit After Tax (norm)	67	(953)	11,258	(142)	(4,496)	(6,221)
Profit After Tax (reported)	(608)	(1,796)	6,651	(992)	(5,312)	(7,124)
Average Number of Shares Outstanding (m)	23.0	23.0	23.3	24.5	28.5	28.5
EPS - normalised (€)	0.00	(0.04)	0.48	(0.01)	(0.16)	(0.22)
EPS - (reported) (€)	(0.03)	(0.08)	0.29	(0.04)	(0.19)	(0.25)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0	100.0	100.0
EBITDA Margin (%)	19.7	N/A	75.0	9.6	N/A	N/A
Operating Margin (before GW and except.) (%)	12.8	N/A	73.4	6.2	N/A	N/A
BALANCE SHEET						
Fixed Assets	18,765	20,128	16,059	18,050	21,170	22,946
Intangible Assets	15,062	15,825	12,928	15,188	18,396	20,291
Tangible Assets	1,485	1,159	981	854	736	618
Investments	2,217	3,145	2,150	2,008	2,037	2,037
Current Assets	3,808	2,851	9,999	22,681	30,848	19,810
Stocks	19	2	9	4	11	8
Debtors	977	663	704	940	1,341	1,140
Cash	2,302	2,033	3,633	19,467	23,875	13,040
Other	510	153	5,654	2,270	5,621**	5,621**
Current Liabilities	(2,283)	(2,724)	(3,969)	(5,296)	(4,552)	(4,102)
Creditors	(765)	(1,005)	(1,299)	(2,401)	(1,432)	(1,737)
Short term borrowings	(1,519)	(1,719)	(2,670)	(2,895)	(3,120)	(2,365)
Long Term Liabilities	(9,949)	(11,251)	(8,196)	(7,841)	(26,952)	(25,882)
Long term borrowings	(7,963)	(9,117)	(6,420)	(6,177)	(24,377)	(23,307)
Other long term liabilities	(1,986)	(2,134)	(1,776)	(1,664)	(2,575)	(2,575)
Net Assets	10,341	9,004	13,893	27,594	20,513	12,772
CASH FLOW						
Operating Cash Flow	1,420	(113)	12,178	1,076	(9,275)	(5,595)
Net Interest	(582)	(672)	(52)	(553)	(993)	(843)
Tax	0	0	0	0	396	0
Capex	0	0	0	0	0	0
Acquisitions/disposals	107	(677)	798	0	0	0
Financing	0	0	0	14,725	0	0
Other	(8,125)	(161)	(9,579)	605	(3,920)*	(2,797)*
Dividends	0	0	0	0	0	0
Net Cash Flow	(7,180)	(1,623)	3,345	15,853	(13,792)	(9,234)
Opening net debt/(cash)	0	7,180	8,803	5,458	(10,395)	3,622
HP finance leases initiated	0	0	0	0	0	0
Other	0	0	0	0	0	0
Closing net debt/(cash)	7,180	8,803	5,458	(10,395)	3,397	12,857

Source: Edison Investment Research, Oryzon Genomics accounts. Note: Oryzon reports in Spanish GAAP. *Represents cash outflows related to development costs that were capitalised. **Term deposits classed as other current assets.

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